

# OPTIMAL FEEDBACK CONTROL AND THE NEURAL BASIS OF VOLITIONAL MOTOR CONTROL

*Stephen H. Scott*

Skilled motor behaviour, from the graceful leap of a ballerina to a precise pitch by a baseball player, appears effortless but reflects an intimate interaction between the complex mechanical properties of the body and control by a highly distributed circuit in the CNS. An important challenge for understanding motor function is to connect these three levels of the motor system — motor behaviour, limb mechanics and neural control. Optimal feedback control theory might provide the important link across these levels of the motor system and help to unravel how the primary motor cortex and other regions of the brain plan and control movement.

Perhaps the most surprising feature of the motor system is the ease with which humans and other animals can move. It is only when we observe the clumsy movements of a child, or the motor challenges faced by individuals with neurological disorders, that we become aware of the inherent difficulties of motor control.

The efforts of systems neuroscientists to understand how the brain controls movement include studies on the physics of the musculoskeletal system, neurophysiological studies to explore neural control, and investigations of motor behaviour (BOX 1). As knowledge continues to grow in each area, it becomes more challenging to link these levels of the motor system and to maintain a cohesive framework within which to describe motor function or to interpret the role of a brain region.

Take, for example, the primary motor cortex (M1). It has been known for more than 100 years that M1 is important for controlling volitional movements, but more detailed statements on its function vary greatly<sup>1</sup>. Studies of neural activity in M1 tend either to relate neural activity to details of motor output, thereby connecting motor cortical function to the motor periphery, or to relate neural activity to hand motion, thereby connecting motor cortical function to the goals of motor behaviour. Which view is correct? Are both correct, and if so, how?

The goal of this review is to bring all three levels of the motor system together, to illustrate how M1 is linked to limb physics and motor behaviour. The key ingredient is the use of optimal feedback control as a model of motor control in which sophisticated behaviours are created by low-level control signals (BOX 2). I begin with a brief review of each level of the motor system, followed by a more detailed description of how optimal feedback control predicts many features of neural processing in M1.

## **Limb mechanics**

The peripheral motor system is a complex filter that converts patterns of muscle activity into purposeful movement. The basic building block of motor output is the motor unit — a motor neuron and the muscle fibres it innervates. The conversion of patterns of motor unit activity into muscle force depends on muscle fibre length, velocity, histochemical type and history-dependencies such as fatigue<sup>2–6</sup>. Muscle force is also influenced by architectural features, including tendon and fascicle length, the orientation of muscle fibres (pennation angle) and passive muscle elasticity<sup>7,8</sup>. Muscle morphometry varies widely even across synergistic muscles<sup>9,10</sup>. The effective joint torque that is generated by a muscle depends on its mechanical advantage (moment arm) about that joint, which often varies with joint angle<sup>11</sup>.

*Department of Anatomy and Cell Biology, Centre for Neuroscience Studies, Queen's University, Kingston, Ontario K7L3N6, Canada.  
e-mail: steve@biomed.queensu.ca  
doi:10.1038/nrn1427*

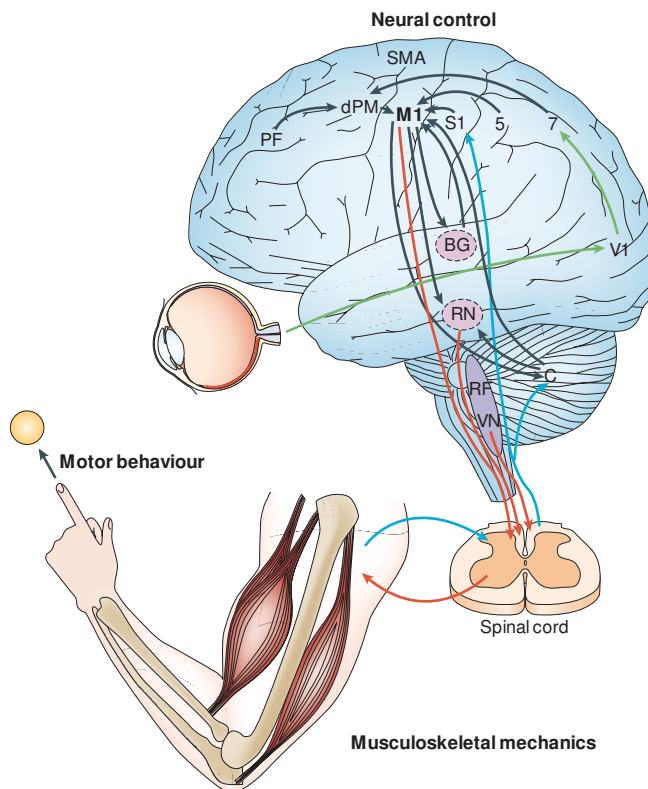
Box 1 | Three main divisions of motor system research

The musculoskeletal system is made up of muscles that act on a multi-articulated skeleton. The translation of limb movement from muscle activity is influenced by muscle and limb mechanics. Motor behaviour describes how the limb or body moves during a motor task, reflecting the combined action of the neural circuit that controls movement and the mechanical properties of the limb. The neural basis of movement examines how different regions of the brain and spinal cord control motor output.

The CNS is generally viewed as having a hierarchical organization with three levels — the spinal cord, brainstem and cortex. The spinal cord is the lowest level, including motor neurons, the final common pathway for all motor output, and interneurons that integrate sensory feedback from the skin, muscle and joints with descending commands from higher centres. The motor repertoire at this level includes stereotypical multi-joint and even multi-limb reflex patterns, and basic locomotor patterns.

At the second level, brainstem regions such as the reticular formation (RF) and vestibular nuclei (VN) select and enhance the spinal repertoire by improving postural control, and can vary the speed and quality of oscillatory patterns for locomotion.

The highest level of control is provided by the cerebral cortex, which supports a large and adaptable motor repertoire. The diagram illustrates some of the key regions that are involved in goal-directed reaching movements. (For more complete details, see REF. 48.) Motor planning and visual feedback are provided through several parietal and premotor regions. The primary motor cortex (M1) contributes the largest number of axons to the corticospinal tract and receives input from other cortical regions that are predominantly involved in motor planning. Somatosensory information is provided through the primary somatosensory cortex (S1), parietal cortex area 5 (5) and cerebellar pathways. The basal ganglia (BG) and cerebellum (C) are also important for motor function through their connections with M1 and other brain regions. (RN, red nucleus; V1, primary visual cortex; 7, region of posterior parietal cortex; dPM, dorsal premotor cortex; SMA, supplementary motor area; PF, prefrontal cortex.)



Skeletal organization has a profound influence on the conversion of muscle forces into limb motion. Limb mechanics are relatively straightforward when movement is constrained to occur at only a single joint and with only one degree of mechanical freedom (flexion or extension). MUSCULAR TORQUE ( $T$ ) is defined simply as  $T = I\ddot{\Theta}$ , where  $I$  equals the moment of inertia, and  $\ddot{\Theta}$  is the angular acceleration of the joint. This angular version of the familiar equation, force = mass  $\times$  linear acceleration, means that there is a direct relationship between joint motion and torque. This simple relationship disappears when movement involves more than one joint. The equations of motion to describe muscular torque at the shoulder ( $T_s$ ) and elbow ( $T_e$ ) are (equations 1,2):

$$T_s = (I_1 + I_2 + m_1c_1^2 + m_2(l_1^2 + c_2^2 + 2l_1c_2 \cos\Theta_e))\ddot{\Theta}_s + (I_2 + m_2c_2^2 + m_2l_1c_2 \cos\Theta_e)\ddot{\Theta}_e - (m_2l_1c_2 \sin\Theta_e)\dot{\Theta}_e^2 - (2m_2l_1c_2 \sin\Theta_e)\dot{\Theta}_s\dot{\Theta}_e \quad (1)$$

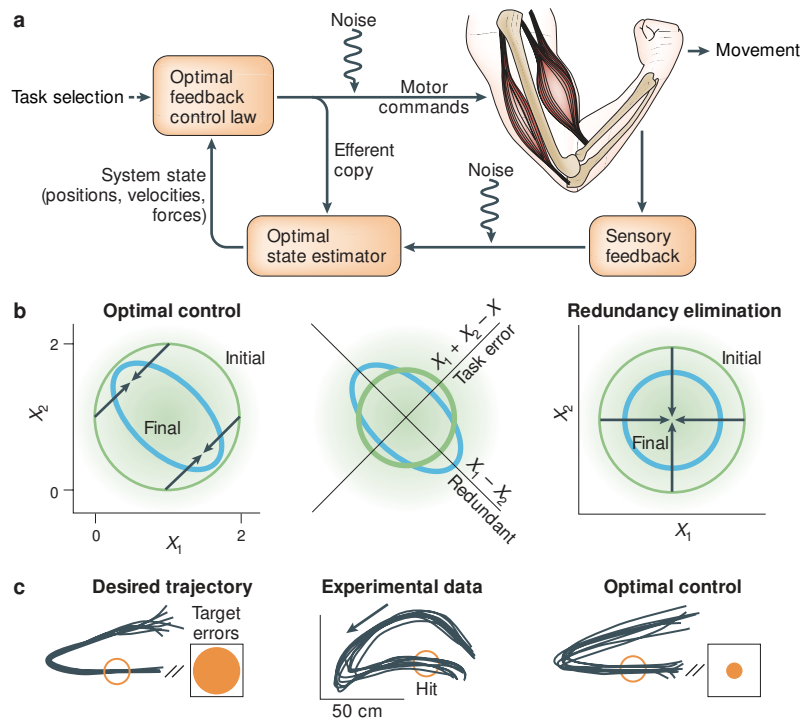
$$T_e = (I_2 + m_2c_2^2 + m_2l_1c_2 \cos\Theta_e)\ddot{\Theta}_s + (I_2 + m_2c_2^2)\ddot{\Theta}_e + (m_2l_1c_2 \sin\Theta_e)\dot{\Theta}_s^2 \quad (2)$$

where  $l_1$  and  $l_2$  reflect properties of the upper arm and forearm/hand, respectively, and  $s$  and  $e$  denote shoulder and elbow, respectively. Muscular torque at a joint depends on several parameters that relate to each segment's moment of inertia ( $I$ ), length ( $l$ ), mass ( $m$ ) and centre of mass ( $c$ )<sup>1</sup>.

These equations of motion mean that there is no longer a one-to-one mapping between joint motion and muscular torque, so that torque at one joint can generate motion at other joints<sup>12,13</sup>. The mechanics of multi-joint movements cannot be predicted from the physics of single-joint movements<sup>14,15</sup> (BOX 3). The equations of motion expand when more joints are involved and when joints have multiple degrees of freedom. Furthermore, a hand-held object or environmental forces such as ground reaction forces during walking

**MUSCULAR TORQUE** (or moment). Each muscle generates force from muscle contraction (active) and elastic forces (passive). Muscular torque for a muscle equals its total force multiplied by its moment arm (the perpendicular distance between a muscle's line of action and the joint centre of rotation).

Box 2 | Optimal feedback control



For a review of this topic, see REF 121. The basic principle of optimal feedback control is that feedback gains are optimized on the basis of some index of performance (see panel a, modified, with permission, from REF 187 © (2002) Macmillan Magazines Ltd). Such controllers correct variations (errors) if they influence the goal of the task; otherwise, they are ignored. Optimal state estimation is created by combining feedback signals and efferent copy of motor commands. The latter uses a forward internal model to convert motor commands to state variables.

A key feature of optimal feedback control can be understood by considering a problem where a system must attain a value of 2.0 using two control signals (b)<sup>38</sup>. Nominally, each control signal could be selected to be 1.0 ( $X_1 = X_2 = 1.0$ ). When these commands are implemented, noise in the system might modify the output such that both signals equal 1.1. The best strategy is to reduce both of the control signals towards 1. In another case, one control signal equals 1.1, but the other equals 0.9. Both values have changed, but the objective to attain a total of 2.0 has been attained, so it is better not to modify the signals. The left diagram illustrates how initial errors in control signals (round circle) are corrected towards a line where  $X_1 + X_2 = 2.0$  (thick oval). The errors show the effects of the control signals at four different initial states, all of which point towards the line that defines the task goal. The right diagram illustrates how initial errors (large round circle) are reduced equally (thick smaller circle) by a traditional controller. Note that the arrows signifying corrective signals all point towards the middle of the circle, the nominal control signals.

The middle diagram compares the final errors of the optimal and traditional controllers. The correct solution falls along the line  $X_1 + X_2 = 2.0$ , and distances perpendicular to this line reflect errors in overall performance. The traditional controller creates the greatest errors and the optimal controller minimizes these larger errors.

Another interesting feature of optimal feedback controllers is that desired trajectories do not need to be planned explicitly but simply fall out from the feedback control laws. The middle panel of c illustrates the trial-to-trial variability of hand motion when subjects hit a ping-pong ball. This variability in performance is lost if a controller is optimal for trajectory tracking, but is captured by an optimal feedback controller that is based on global task errors.

can markedly influence limb mechanics<sup>13</sup>. This article largely focuses on proximal-arm movements, but there are more challenging mechanical problems for hand<sup>16,17</sup> and orofacial<sup>18</sup> motor function.

Motor behaviour

Body movements are smooth, despite the complexities of the peripheral motor system. For example, hand trajectories remain relatively straight from start to end, and hand velocity follows a smooth, bell-shaped profile<sup>19,20</sup> (FIG. 1). This smoothness at least partially reflects the low-pass filter properties of muscle<sup>21</sup>. Perturbations of the hand during slow movements are corrected back towards the unperturbed trajectory, indicating that feedback is used to maintain a relatively straight hand trajectory, at least under these conditions<sup>22</sup>. Such simple features of hand motion mean that the CNS compensates for the complexities of limb mechanics.

The motor system can also adapt to changes in the mechanical environment. Lackner and DiZio<sup>23</sup> observed how subjects performed reaching movements before, during and after they sat in a room that rotated at 6 rpm, creating a coriolis force on the limb. When subjects performed their first reaching movements with the right arm in the rotating room, after the otolith organs no longer sensed room rotations, the movements were curved to the right. However, after several trials, reaching movements returned to relatively straight trajectories, similar to those seen before the room began to rotate. When the room stopped rotating, initial reaches were curved to the left, and subjects perceived that a strange force had pushed their limb. Again, reaching movements quickly returned to near straight trajectories. When a hand-held robot applied loads during reaching, the results were similar<sup>24</sup>. Many studies have shown that relatively straight hand trajectories are preserved after various perceptual and mechanical perturbations<sup>25–28</sup>.

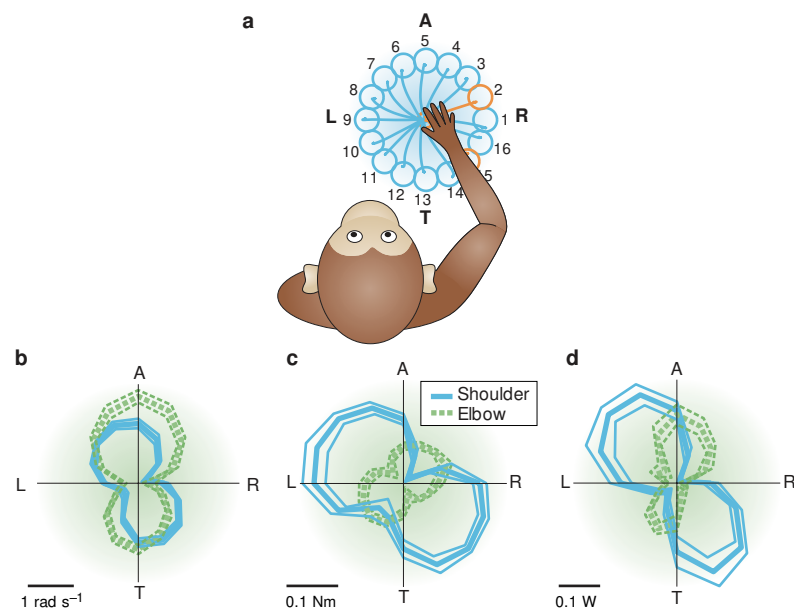
Although movements are smooth, motor performance shows considerable trial-to-trial variability, which partially reflects inherent noise in the system related to both sensory and motor signals<sup>29–31</sup>. However, some features of motor performance, particularly task-relevant features, are tightly controlled<sup>32–34</sup>. For example, fluctuations in joint configurations that influence the orientation of a subject pointing a laser at a spatial target are reduced, whereas patterns that do not influence laser orientation are more variable<sup>35</sup>. There is a growing body of literature that illustrates how the motor system considers the influence of noise and variability in motor planning and control<sup>36–40</sup>.

Motor behaviour shows several key features. Movements are smooth, highly adaptable and show selective patterns of variability that reflect economy of task-relevant features of motor performance. In spite of the complexities of limb mechanics, a hallmark of motor performance is smooth and relatively straight hand trajectories.

Neural centres of sensorimotor control

Sensorimotor function is created from a highly distributed circuit that includes the spinal cord, brainstem and cerebral cortex (BOX 1). The spinal level supports the ‘most automatic’ movements, including reflexes, as well as more complex multi-joint and multi-limb sensorimotor responses. The cortex supports the

## Box 3 | Complexities of multi-joint movements



Point-to-point reaching movements are quite simple with regards to the motion of the hand in space. Hand motion is relatively straight for reaching movements in different spatial directions (panel a). Hand movements with similar magnitudes but in different directions produce large variations (anisotropies) in the magnitude of joint motion, torque and power.

Panel b shows a polar plot where direction defines the spatial direction of hand motion and the distance from the origin reflects the magnitude of joint motion. Angular velocity is greatest at the shoulder (blue) and elbow (green) for movements towards or away from the monkey, whereas angular motions are small for movements to the right and left. This variation in joint motion for different directions of movement is a property of limb geometry. The magnitude of angular motions vary with limb position so that movements starting from a more extended posture create larger anisotropies in joint motion, whereas starting positions closer to the body are less anisotropic. Variations in muscular torques do not simply follow the patterns of joint motions. Peak muscular torque at the shoulder is greatest for movements to the left and away, and towards and to the right, whereas elbow muscular torque is greatest for movements in the opposite quadrants (c). The magnitude of angular motions at the shoulder and elbow are fairly similar, but there is a large difference in the magnitude of shoulder and elbow muscular torque. Joint power — joint angular velocity multiplied by muscular torque — reflects the amount of energy that is transmitted to the limb from muscles at each joint (d). Peak torque is greatest at the elbow for movements away from and towards the body, whereas it is greatest at the shoulder for movements in a more clockwise direction. Nm, Newton metres; Rad, radians; W, Watts.

Modified, with permission, from REF 15 © (2003) American Physiological Society.

‘most voluntary’ motor tasks, such as reaching for an object of interest, and learned associations, such as stepping on the car brake when a traffic light turns red. Voluntary behaviours often include more automatic components — for example, a voluntary reach of the hand to a spatial target invokes automatic postural adjustments to stabilize the body.

Neural recordings from monkeys are often used to examine how the activity of individual neurons relates to sensorimotor function. The anatomical and physiological properties of the limbs<sup>9,41</sup> and CNS are similar across primates<sup>42,43</sup>, and species such as *Macaca mulatta* can learn sophisticated motor behaviours (see, for example, REFS 44–46).

The activities of the cerebral cortex can be divided into two general problems in motor control — planning and execution. Motor planning reflects a range of issues that are related to the identification and selection of goals and strategies. Several cortical regions, including many parietal and frontal regions, participate in motor planning<sup>47–51</sup>.

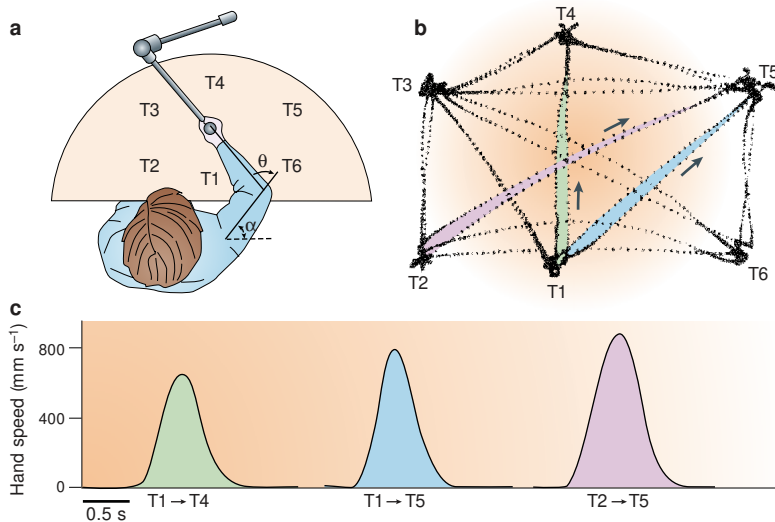
By contrast, M1 is more important for the execution of goal-directed and skilled motor tasks<sup>42,43</sup>. Lesions of M1 in monkeys initially cause severe difficulties in voluntary movement, which remain permanent for more challenging distal limb motor tasks<sup>52</sup>. M1 has an intimate relationship with the motor periphery. It receives a rich mixture of sensory feedback from the motor periphery, with many neurons responding strongly to passive joint movements or skin contact. Most descending signals from the cortex pass through spinal interneurons<sup>53</sup>. However, some neurons in M1 (corticomotor (CM) neurons) form synaptic connections directly onto spinal interneurons<sup>54–56</sup>, allowing M1 to have a more direct and selective influence on muscle activity. CM neurons are more prevalent for distal limb musculature related to the hand<sup>42,57</sup>, and their numbers and influence increase with the level of dexterity across primate species<sup>58,59</sup>.

### Bridging the gaps

The discussion above describes three features of the motor system. First, the physics of moving even two joints is complex. Second, humans can generate a range of skilled motor tasks. In reaching tasks, the trajectory of the hand tends to be conserved across conditions, but there is also considerable trial-to-trial variability in the path of the hand. Third, motor control is created by a distributed and interconnected circuit in which M1 has a crucial role for volitional, goal-directed tasks. An important problem is to understand the links between motor behaviour, limb mechanics and neural control. How do neural circuits create purposeful movements from the complex, nonlinear musculoskeletal system? Does the neural activity of M1 reflect the control of high-level features related to behavioural goals, or of low-level features related to the motor periphery? In effect, this question reflects the age-old problem: does the primary motor cortex code muscles or movements?

**M1 and motor behaviour.** Relatively straight hand trajectories and bell-shaped velocity profiles during reaching indicate that the motor system might directly control hand motion<sup>20,22,60,61</sup>. Neural signals in some brain region(s) would explicitly signal hand trajectory, and these commands would be converted into patterns of muscle activity, potentially through intermediate representations<sup>62,63</sup>. For the online control of hand motion, proprioceptive signals would need to be converted from muscle to hand space, but it would be relatively simple to compute from vision.

The idea that hand trajectory is controlled online is consistent with electrophysiological recordings from M1 in non-human primates during whole-limb movements. More than 20 years ago, Georgopoulos and



**Figure 1 | Features of motor behaviour.** **a** | Morasso<sup>19</sup> illustrated several key features of how humans made point-to-point reaching movements in the horizontal plane using a mechanical linkage to monitor motion of the hand in space.  $\alpha$  and  $\theta$  denote shoulder and elbow joint angles, respectively. **b** | Trajectories of the hand between the spatial targets (T1–T6) are relatively straight from the start to end of movement. **c** | The velocity of the hand shows a characteristic bell-shaped profile with peak hand velocity proportional to movement distance. Modified, with permission, from REF. 19 © (1981) Springer-Verlag.

colleagues trained monkeys to make whole-limb reaching movements in different directions, and related neural activity to hand motion<sup>64</sup>. The activity of individual neurons in M1 was broadly tuned to the direction of hand motion — activity was maximal for motion in the cell's preferred direction, and decreased progressively for movements away from this (FIG. 2). A population vector that compared activity across the ensemble of recorded neurons could predict the direction of hand movement<sup>65</sup>. Subsequent studies have shown that neural activity in M1 correlates with many hand-related variables, including hand direction, speed and movement distance<sup>66,67</sup>. Neural correlates of hand motion are found in parietal area 5 (REF. 68), the primary somatosensory cortex<sup>69</sup>, the dorsal premotor cortex<sup>66,70</sup>, the cerebellum<sup>71</sup>, the dorsal spino-cerebellar tract<sup>72</sup>, muscle afferents<sup>73,74</sup> and even proximal-limb muscle activity<sup>75,76</sup>. It has been suggested that neural activity related to hand motion provides a higher-order common language that allows M1 to communicate with other brain regions<sup>77</sup>.

Although neural correlates of hand motion in M1 provide an important link to motor behaviour, it leaves the spinal cord with the problem of converting these high-level signals into patterns of muscle activity<sup>78</sup>. In theory, the spinal cord could support a mapping between hand motion and proximal-limb muscle activities. The spinal cord can create complex multi-joint and multi-limb reflexive motor responses<sup>79–81</sup>.

However, a key feature of volitional motor control is the ability to adjust motor patterns on the basis of the behavioural context. In addition, loads can be applied anywhere on the body. Therefore, if some descending commands to the spinal cord specified the kinematics of hand motion, other descending signals would be required to consider environmental forces.

A lively debate remains on the interpretation of correlates of hand motion taken from neural activity in M1 (REFS 82–85). Theoretical studies have shown that neural activity can predict the direction of hand motion even if neurons code other details of motor performance such as muscle activity or joint motion<sup>86–88</sup>. As described below, neural activity correlates with many features of movement other than hand motion. Furthermore, recent studies in which reaching movements were performed with the arm in the horizontal plane found that population vectors did not always predict the direction of motion<sup>89,90</sup> (FIG. 2). Population vectors tended to be skewed either away from and to the left of the monkey, or towards and to the right of the monkey. Vector length varied substantially even though hand velocity remained invariant across spatial directions.

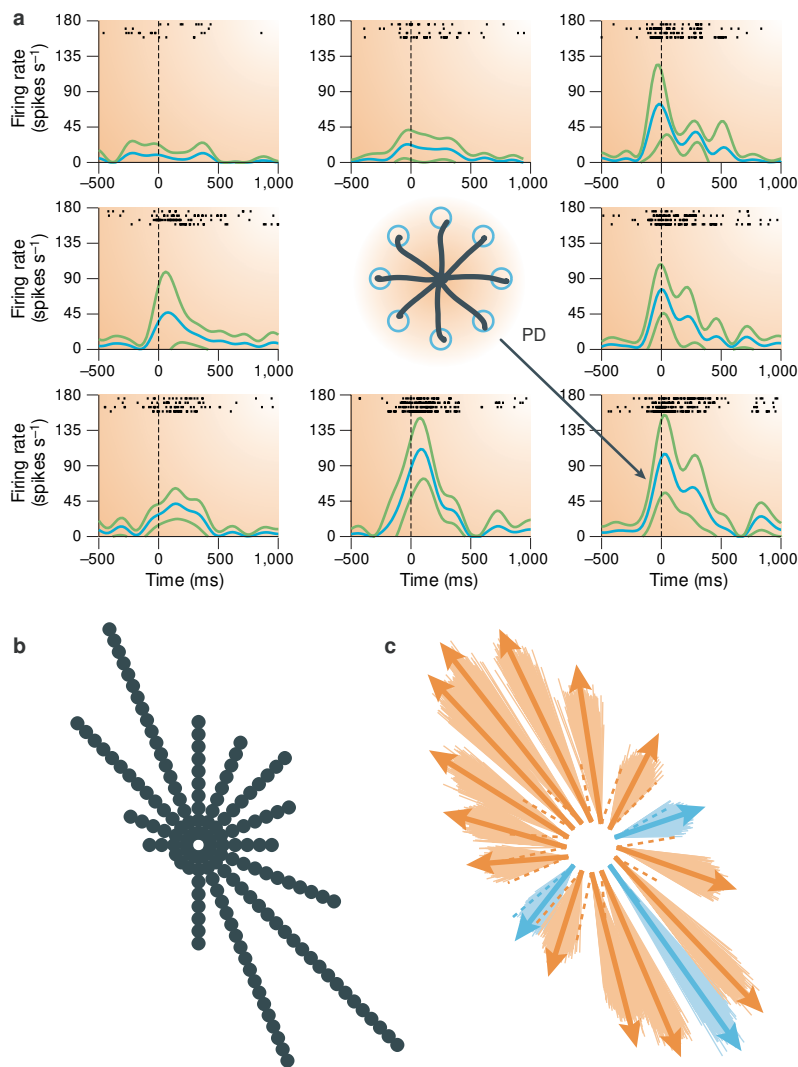
Clearly, for monkeys to reach to spatial targets, population vectors are not required to point in the direction of hand motion. More accurate mathematical techniques can be used to predict hand motion<sup>88</sup>, but such techniques can predict almost any other variable of movement. Estimates of hand direction can be computed from shoulder and elbow muscle activity<sup>87</sup>, but that does not mean that these muscles directly control hand motion beyond the obvious link between muscular force and limb motion.

Although concerns have been raised regarding the importance of neural correlates of the direction of hand motion in M1, such correlates remain appealing because they directly link neural processing in the brain to a key feature of motor behaviour<sup>34,60–62</sup>.

**M1 and the motor periphery.** A second stream of research relates neural processing in M1 to the motor periphery. This approach can be viewed within the framework of internal models, neural processes that mimic the properties of the limb or the environment<sup>23,24,91</sup>. Such models reflect the association between motor commands and limb movement, or vice versa. The concept of internal models has been particularly influential for studying human sensorimotor control and motor learning.

There is evidence that M1 behaves like or forms part of an inverse internal model, converting spatial goals or hand trajectories into detailed motor patterns to control the limb musculature<sup>50,92</sup>. Such a framework explains many of the characteristics of neural activity in M1, such as correlations with patterns of muscle activity<sup>93,94</sup>. More importantly, activity in M1 before the onset of movement is altered by peripheral factors such as the position of the limb in space<sup>70,95</sup>, arm geometry<sup>76</sup>, joint power<sup>89</sup> and force output<sup>45,75</sup>. All of these provide correlates of an internal model for initiating movements.

Although the concept of internal models helps to link M1 activity and function to the management and control of limb mechanics, this framework is rather vague. It helps to explain why M1 activity reflects many of the features of the motor periphery, but it does not explain how the brain can create emergent behaviour such as relatively straight hand paths and bell-shaped velocity profiles. Some neurons in M1 reflect features of



**Figure 2 | Neural activity in primary motor cortex (M1) during reaching.** **a** | Mean hand trajectory is shown in the central panel for movements to each of eight spatial targets surrounded by the corresponding response of the neuron for each target. The rasters at the top of each panel illustrate the times of action potentials for five trials. Data are aligned to movement onset (vertical dashed line). Below each raster are the mean (blue) and standard deviation (green) of the discharge rate of the neuron for each movement direction. The large black arrow denotes the preferred direction (PD) of the neuron. **b** | Distribution of preferred directions of neurons in M1. Each dot denotes the preferred direction of an individual neuron. Distribution is based on neural activity only during the reaction time period, although similar results were found for any epoch during reaction and movement time. ( $n = 154$ ,  $P < 0.001$ .) **c** | Population vectors based on reaction time activity of neurons are denoted by arrows with their base attached to the corresponding direction of hand motion for the initial 100 ms of movement (dashed line). Orange and blue arrows denote whether the difference between the direction of hand motion and the population vector is significant or insignificant, respectively. Under each population vector is the dispersion of vectors formed by random resampling of the cell population with replacements. Modified, with permission, from REF. 90 © (2003) Elsevier Science.

#### EQUILIBRIUM POINT MODELS

A class of models that assume the CNS can control the equilibrium position established by the balance of force that is generated by the spring-like behaviour of muscle.

movement such as target or hand direction<sup>95,96</sup>. Is this proportion of neurons sufficient to provide online control of the hand?

If M1 considers limb mechanics, perhaps other cortical regions support on-line control of hand motion. However, candidate regions tend to be more involved in planning than motor execution. Lesions in the dorsal premotor cortex or supplementary motor

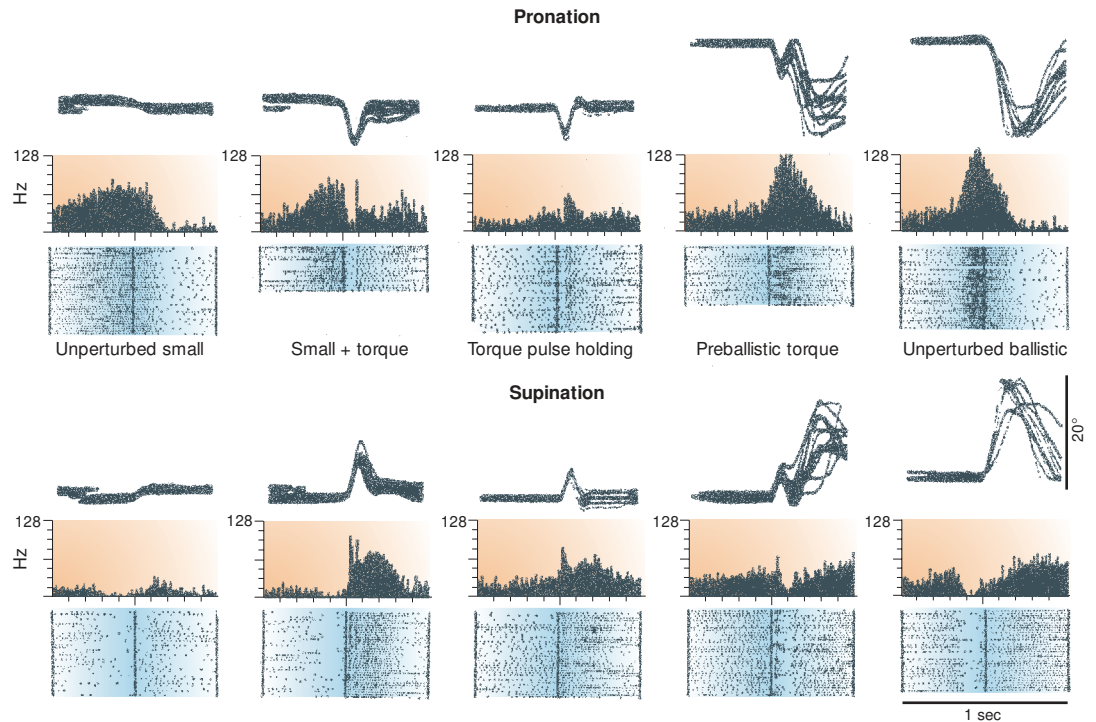
cortex create deficits in decisional processes and strategies of motor action rather than in online control<sup>97–101</sup>. Motor actions are still coordinated, but are either delayed in execution or inappropriate for the behavioural context. With regards to online control, temporary inactivation of the supplementary motor area has no substantial effect on M1 activity or on behavioural responses to perturbations applied to the wrist<sup>101</sup>.

After 40 years of single-cell neural recordings in monkey M1, there is evidence that M1 neurons can code anything from hand direction to detailed patterns of muscle activity<sup>90</sup>. Such diversity might be a key feature of M1 function, reflecting a number of sensori-motor transformations<sup>62,63</sup>. As described above, neural processing in M1 is consistent with its role as part of an internal model that converts global goals into motor commands to the periphery<sup>50,92</sup>. However, both of these frameworks provide descriptions of neural activity rather than a formal control theory for limb motor control.

The oculomotor field has identified in detail many features of the motor circuitry that is involved in eye and gaze control<sup>102,103</sup>. The oculomotor system lacks much of the complexity of limb motor function, and the activity of motor neurons and pre-interneurons in the brainstem can be recorded. However, another key to the success of these studies is that they took advantage of formal control models to guide experimental work<sup>104,105</sup>. Similar control models were introduced to characterize limb movement and neural circuitry predominantly in the spinal cord<sup>106</sup>, but they are limited in their ability to reflect the complex anatomical and physiological properties of neural circuits even at this level<sup>107</sup>, let alone as a useful model of brain function related to volitional movement control. EQUILIBRIUM POINT MODELS incorporate the use of spinal stretch reflexes in descending commands<sup>108</sup>, but cannot explain end-point errors induced by applied loads<sup>23,24,109</sup> and again do not consider supraspinal processing. Some models have been developed to interpret the role of specific cortical regions and the patterns of activity of their constituent neurons for specific tasks, such as goal-directed limb movements<sup>110,111</sup>, but they do not replicate the natural patterns of variability in motor output.

#### Optimal feedback control

Optimal control has been used to interpret motor behaviour by optimizing motor commands for some aspect of motor performance (such as maximal jump height or minimal end-point errors)<sup>30,112–116</sup>. Optimal feedback control modifies feedback signals to optimize an index of performance, creating a complex link between sensory signals and motor output (BOX 2). It has been used to interpret various motor behaviours, including spinal reflexes in the cat hindlimb<sup>117</sup>, human postural balance<sup>118</sup> and volitional motor control<sup>38,119</sup>. The ability of the motor system to adapt and use various sensory signals for feedback control is exemplified by our ability to use cutaneous signals from light finger contact to stabilize standing posture<sup>120</sup>.



**Figure 3 | Response of a primary motor cortex (M1) neuron to mechanical perturbations in different contexts.** Each panel illustrates wrist position, the instantaneous firing rate and a raster display of the response of the neuron in individual trials. The top row of panels shows responses for pronation movements and loads, and the bottom row of panels shows responses for supination movements and loads. Each column illustrates the response of the neuron in a different context, as defined in the diagram. Note the change in the response of the neuron to mechanical loads applied when generating a small movement (small + torque), when holding a fixed position (torque pulse holding) and at the start of a large movement (preballistic torque). Reproduced, with permission, from REF. 139 © (1978) Karger.

An optimal feedback controller has several key components<sup>121</sup>. First, optimal control needs an optimal estimate of the state of the system (STATE VARIABLES), which is generated from afferent feedback from sensors combined with efferent copy of motor signals. In humans, both afferent feedback and efferent copy are used to estimate ongoing motor performance<sup>122</sup>. Support for the use of efferent copy in motor control is provided by observations that motor commands can undergo rapid compensation before sensory feedback can influence them<sup>123</sup>. State variables can reflect not only the properties of the body, but also information related to grasped objects<sup>116</sup>.

Second, feedback gains to convert these state variables into motor signals are not fixed, but are adjusted based on the specific goals of a behaviour. This is essentially an optimization problem that manipulates feedback gains to maximize or minimize some index of performance. A property of optimal feedback controllers is that sensed variations in state variables lead to corrections if they adversely affect motor performance, but are ignored if they do not. Todorov and Jordan<sup>38</sup> define this as a 'minimum intervention' principle. This selective correction of errors is particularly important for a system with noise, which is prevalent in both motor output<sup>30</sup> and sensory signals<sup>29,31</sup>.

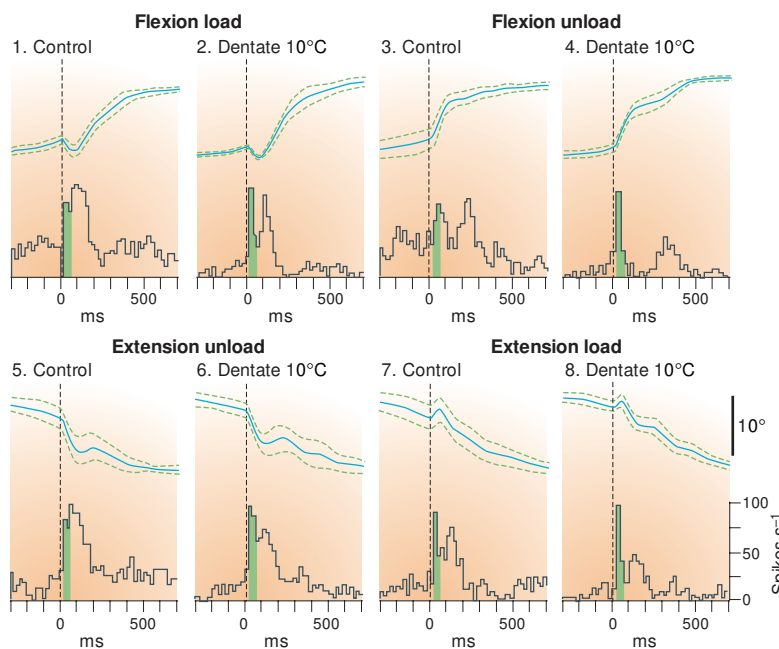
By its nature, optimal control modifies feedback gains to suit the overall goals of the system. These gains

can vary with time, as observed for peripheral feedback during locomotion<sup>124</sup>. Todorov and Jordan<sup>38</sup> have proposed that such flexibility in the properties of the controller might be a valuable conceptual framework for interpreting volitional motor behaviour such as reaching and grasping. They show that such a controller captures many of the common features of human movement, including goal-directed corrections, multi-joint synergies and variable but successful motor performance. Several features of motor performance emerge despite not being explicitly defined in the feedback controller.

The observation that reaching movements are relatively straight with bell-shaped velocity profiles provides strong circumstantial evidence that the CNS directly controls hand trajectory. However, hand trajectory does not have to be directly controlled if the brain behaves like an optimal feedback controller. Behavioural goals (such as reaching to a spatial target) can be converted directly into feedback laws to convert state variables into motor commands. Hand motion simply falls out as the optimal controller adjusts motor output on the basis of statistical variations in state variables created by external perturbations and system noise. Errors that influence the goal of the task are corrected, those that do not are ignored. Even if hand trajectory itself becomes the goal of a task such as slow reaching<sup>22</sup>, it does not need to be explicitly defined in the controller.

STATE VARIABLES

Estimates of the position of the limb or forces acting within or on the limb (or their derivative). State variables are transformed by corresponding feedback gains to generate motor output commands.



**Figure 4 | Effects of dentate cooling on the discharge pattern of a primary motor cortex (M1) neuron.** Flexion or extension loads are either abruptly applied or removed at the start of either flexion or extension movements under control conditions (conditions 1, 3, 5 and 7). Each panel illustrates elbow motion (mean, blue solid line, and standard deviation, green dashed line) and the instantaneous firing rate of the neuron. Conditions 2, 4, 6 and 8 are the corresponding movements and cell discharge pattern when the dentate nucleus was cooled temporarily. Note that the early response of the M1 neuron (green column) remains the same before and during cooling, but the later response started 20 ms after the perturbation is altered with dentate cooling. Reproduced, with permission, from REF. 144 © (1975) Elsevier Science.

This property of optimal feedback controllers greatly changes the expected computational processes performed by the motor system. There is no need to convert neural signals explicitly into a representation of hand motion for motor execution. Therefore, the neural correlates of hand motion that can be found throughout the sensorimotor system might simply be epiphenomena<sup>125</sup>.

Not only does hand trajectory not need to be explicitly computed, neither do any other intermediary representations. The distribution of muscle afferents do not seem to be optimal for any specific representation of limb position<sup>29</sup>. If there are no substantive restrictions on the state variables used by the controller, signals related to the motor periphery could simply reflect their natural coordinates. For primary muscle spindles, natural representation is a combination of muscle length and velocity. Convergence of various receptors would create rich, but low-dimensional state variables and the motor system would develop feedback laws to act on these signals.

#### **Implications of optimal feedback control for M1.**

If optimal feedback control is a useful computational theory for describing volitional motor control, it might also be valuable for interpreting the neural basis of volitional motor control. This control theory is consistent with several features of neural processing in M1, including neurons that reflect only part of the motor apparatus, and rich afferent feedback that is adaptable based on behavioural context.

Optimal feedback control that is based on low-dimensional state variables is consistent with the most obvious feature of M1 — a coarse somatotopic representation of the motor periphery with neurons related to one or a few joints<sup>126,127</sup>. Selective changes in mechanical loads applied to the elbow or shoulder joints during posture and movement illustrate that some neurons are sensitive to loads at both joints, whereas others respond to loads at only one joint<sup>45,128</sup>. Corticomotor neurons synapse on motor neurons from a few muscles that span one or more joints<sup>54,57</sup>. These observations indicate that neurons are exclusively associated neither with the entire limb nor with a single joint. Rather, neurons reflect a portion of the motor periphery that might or might not span multiple joints.

Like M1, an optimal feedback controller should receive a rich mix of sensory signals (for review, see REFS 42,43). Many neurons in M1 respond to passive movement of one or more joints<sup>76,129</sup>, and this sensory feedback often overlaps with their motor output<sup>76,130,131</sup>. Many neurons respond to passive and active movements at multiple joints, but the association between these sensory and motor representations remains poorly understood. Neurons related to the distal limb often respond to passive movements of the wrist and digits, or to cutaneous stimulation on the hand, reflecting the importance of cutaneous input for hand function<sup>132–134</sup>. Neurons in shoulder-related regions of cat M1 often have cutaneous receptive fields on the paw<sup>135</sup>, reflecting the link between walking surface stability and proximal muscle control for quadrupedal locomotion.

As expected for feedback control, M1 neurons respond quickly to limb perturbations. Many neurons respond within 20 ms, only slightly slower than the primary somatosensory cortex<sup>136,137</sup>. More importantly, neural responses in M1 can be modified by behavioural context, as predicted by optimal feedback control theory. Sensory responses to passive limb movement can be viewed as a default pattern of sensory feedback and there seems to be almost an equal proportion of neurons with the same or opposite responses for active and passive movements at a joint<sup>138</sup>. However, such passive responses seem to be modifiable, as 90% of 'sensory' responses to mechanical perturbations applied during posture are opposite to their responses for active movements<sup>139</sup>. This provides only indirect evidence that the responses of neurons to sensory stimuli are altered depending on context (passive motion versus actively maintaining a constant limb position). FIGURE 3 shows another example of changes in M1 activity with behavioural context<sup>139</sup>. The responses of M1 to load vary depending on whether the monkey is trying to maintain a constant joint position or is making a small or large movement. Although such studies illustrate the adaptability of neural responses to mechanical perturbations, it remains to be verified whether and how such changes reflect an optimal strategy. More complex changes in the response to sensory feedback are predicted by optimal feedback control, particularly for multi-joint motor tasks that create broader and richer behavioural goals.



Long-latency muscle responses (> 60 ms), which are generated largely through the transcortical pathway<sup>140</sup>, illustrate the potential capability of this feedback system<sup>141</sup>. When the limb is perturbed from a stationary position, the short-latency muscle response (< 60 ms) that is generated at the spinal level parallels the pattern of joint motions (the simple stretch reflex). By contrast, the long-latency response produces the requisite motor patterns to oppose the load, indicating that the transcortical pathway considers the influence of intersegmental dynamics in converting sensed limb motion into compensating motor responses. Furthermore, this long-latency response is modified to incorporate the influence of mechanical loads during motor learning<sup>142,143</sup>.

Several brain regions project to M1 and probably provide feedback from the motor periphery, including the primary somatosensory cortex, posterior area 5 and thalamic input from the cerebellum through the interpositus and dentate nuclei<sup>42</sup>. The earliest response in M1 during mechanical perturbations seems to be provided by the primary somatosensory cortex, as dentate cooling does not influence these early responses<sup>144–146</sup>. However, interpositus neurons respond to mechanical loads within 20 ms (REF. 147). Later responses in M1, starting about 60 ms after a perturbation, seem to be strongly influenced by the cerebellum<sup>145,148</sup> (FIG. 4). How these different pathways contribute to feedback control through M1 and the brainstem regions remains an important problem.

The description above integrates feedback from the motor periphery into motor cortical function, but visual feedback is also important for volitional motor control<sup>149–151</sup>. A proportion of neurons in M1 signal movement or target direction independent of arm configuration<sup>76,95,96,152</sup>. They are often assumed to provide a higher-level representation of movement related to the spatial direction of movement, but such activity might also signal visual feedback of motor performance. Such feedback signals of hand motion are computationally equal and not hierarchically above feedback signals from the motor periphery that are 'muscle-like'. Furthermore, visual feedback is highly task dependent. For example, when writing with the tip of the elbow in space, visual feedback of motor performance would reflect elbow and not hand motion. Although vision is important for online feedback<sup>153,154</sup>, loss of proprioception has a more profound effect on coordinated body movements<sup>155–157</sup>.

The 'transcortical servo' hypothesis that was put forward by Phillips more than 30 years ago emphasized the importance of feedback signals in motor control and was influential in the 1970s for interpreting motor cortical function on the basis of single-joint movements<sup>158</sup>. The predominant use since the 1980s of a whole-limb reaching paradigm to study motor behaviour, and the practice of relating neural activity to hand motion, opened up issues related to the use of vision for action, motor planning and the early, feedforward stage of motor execution. The value of optimal feedback control as a computational theory is that it brings these largely distinct fields of study back together, recognizing

the importance of sensory feedback to M1 processing with more recent advances on multi-joint mechanics, motor behaviour and motor planning.

**Optimal feedback control beyond M1.** A complete description of how optimal feedback control can be applied to other brain regions is beyond the scope of this review, but there are a few issues worth noting. Optimal feedback control makes an important distinction between motor execution and motor planning. This segregation between control and goals seems to be reflected in the cortex, with M1 being more involved in the former, and other frontal and posterior parietal regions being more involved in the latter<sup>50</sup>. However, the segregation is not complete; neural activity during motor preparation can be observed in M1 (REFS 152,159) and at the spinal level<sup>160</sup>.

Visual signals transmitted through the posterior parietal cortex are important for motor planning and the online control of movement<sup>153,154,161,162</sup>. Therefore, the posterior parietal and premotor cortex might be involved in both planning and online control, with individual neurons participating in both processes<sup>163</sup>.

State variables that are based on visual feedback (and probably other sensory signals) seem to be modifiable. For example, after a monkey has been trained to use a rake to grab food morsels, neurons in the intraparietal sulcus that normally respond to visual stimuli near the hand now also respond to stimuli near the rake<sup>46</sup>. Such plastic changes in vision-related neural responses might explain how humans and monkeys can easily use computer-based visual feedback to control motor actions.

Subcortical networks through the basal ganglia and cerebellum are also important for sensorimotor control. In particular, the cerebellum has long been associated with motor control, coordination and learning<sup>91,164–167</sup>, and almost certainly has a crucial role in online feedback control. Damage to this structure leads to motor problems for tasks that involve multiple joints<sup>164,168</sup>. The anatomical and physiological properties of the cerebellum are consistent with several aspects of optimal feedback control. The interpositus nucleus and intermediate cerebellum receive proprioceptive feedback on motor performance from the ascending spinocerebellar tracts and also receive a strong projection from M1 through the pontine nuclei. This mixture of afferent signals and efferent copy provides the ideal conditions for optimal state estimation related to the motor periphery<sup>91,169</sup>. The dentate nucleus and lateral cerebellum are also probably involved as part of an optimal feedback controller. Several frontal and parietal cortical regions project to and receive input from the dentate nucleus through the pontine and thalamic nuclei, respectively<sup>165</sup>. However, each cortical region projects to largely separate regions of the dentate nucleus and cerebellar cortex, creating distinct cerebrocerebellar loops<sup>170,171</sup>. Each of these loops might participate in distinct processes including task selection (motor planning), optimal state estimation and feedback control. Monkeys trained either to assist or to resist

a perturbing flexor load applied to the wrist show context-dependent changes in neural activity in M1. A neuron might fire in a rapid burst when a load is applied if the behavioural condition was to resist the load, but would be unresponsive when instructed to assist the applied load<sup>172</sup>. Similar coupling to instructional cues is also observed in the dentate nucleus<sup>147</sup>, indicating that the dentate nucleus might be involved in rapidly switching from one context to another.

Descending commands from M1 and other brain regions must consider more than just ALPHA MOTOR NEURON activity during motor function<sup>90</sup>. GAMMA MOTOR NEURON activity and the inflow of sensory signals for motor output, and transmission to supraspinal centres for both control and perception are also important. A substantial proportion of corticospinal axons terminate in the intermediate horn and even the dorsal horn<sup>42</sup>. These other features of spinal processing might account for half of the descending signals from the cortex, but little is known about the nature of such signals<sup>173</sup>. If the brain behaves like an optimal feedback controller, it might be best to view descending commands as controlling the spinomusculoskeletal system, rather than the musculoskeletal system<sup>174</sup>.

### Things to do and not to do

There might be many ways to use optimal feedback control to guide neurophysiological research, although several challenges remain. First, the mathematics that is required to identify optimal feedback control laws is extremely challenging even for the simplest of linear systems. This limits the conditions under which formal solutions can be used to predict the properties of an optimal feedback controller, although recent mathematical advances might extend this approach for nonlinear systems<sup>175</sup>. Further theoretical work is also required to break down the processes of optimal feedback control into more biologically plausible algorithms and processes<sup>176</sup> that can help to guide experimental studies. However, it is unlikely that such efforts will attain the level of detail that is present in oculomotor models of brainstem circuitry.

Identifying state variables would be a logical start for examining neurophysiological correlates of optimal feedback control. On its own, this is probably the least informative exercise and simply continues the basic practice of correlating neural activity in M1 and elsewhere with engineering-inspired variables. The rich mix of sensory signals (cutaneous, muscle proprioceptors and vision) that are used to guide motor function obfuscate any simple unified representation. Further diversity is expected in a region such as M1 owing to its interaction with various cortical and subcortical brain regions<sup>90</sup>. Although neural activity must be quantified relative to some measured (or estimated) variable, relative changes within and across task conditions are far more informative than interpreting absolute levels of neural activity.

The important feature of optimal feedback controllers is that they are malleable systems defined by behavioural goals so that variations in sensory or motor

signals will have crucial consequences in one behavioural context and be irrelevant in another. If the long-latency muscle response reflects the feedback laws of an optimal feedback controller, then transient perturbations during different tasks should elicit behaviourally relevant motor responses. Neural recordings in various brain regions will help to disseminate how such feedback control laws are created by the highly distributed motor system.

The mathematics of optimal feedback control are particularly challenging. The brain does not implement the formal mathematical methods that are available to compute gains of optimal feedback controllers, but how neural networks create and learn these properties is an interesting and important process<sup>177–179</sup>. M1 is intimately involved in motor learning, and many studies have investigated plasticity and changes in neural processing in M1 during learning and adaptation<sup>180–183</sup>. Optimal feedback control requires substantive learning at two points in the controller, one for optimal state estimation and the other for optimal control laws. The learning rules and mechanisms are different for these two processes, with the former optimizing estimates of the state of the system, independently of behavioural goals. By contrast, the latter must also use more global rewards that are related to behavioural success or failure.

The motor system is not just one big feedback loop; rather, it is highly distributed and provides multiple pathways through which feedback can influence behaviour. Besides M1, several other brain regions contribute to descending signals to influence spinal processing<sup>53</sup>. Two regions that might be of particular interest for feedback control are the magnocellular red nucleus, which projects to the spinal cord and receives substantive input from both M1 and the cerebellum<sup>165,184</sup>, and area 3a in the primary somatosensory cortex, which receives substantial input from muscle proprioceptors and projects to the intermediate and ventral horn of the spinal cord<sup>137,185</sup>.

Where and how visual and proprioceptive signals are integrated for estimating state variables and feedback control laws at the single-cell level remains poorly understood. Clearly there is substantive integration of different sensory systems for position sense and kinaesthesia<sup>186</sup>. Visual feedback is assumed to take predominantly a cortical path to M1 through the parietal and premotor cortex<sup>48</sup>. There are several potential pathways for proprioceptive feedback to reach M1, including through the primary somatosensory cortex, posterior parietal area 5 and the cerebellum<sup>42</sup>. As stated earlier, somatosensory feedback could be integrated with visual signals in posterior parietal regions and then transmitted through the premotor cortex. However, it is not clear how each of these pathways is involved in motor execution, learning or both.

### Summary and conclusions

The aim of this review was to bring together three levels of research on limb motor function — the motor periphery, motor behaviour and the neural basis of movement. Each level provides a unique perspective on the characteristics of the motor system, and an important challenge in systems neuroscience is to connect

ALPHA MOTOR NEURON  
Motor neurons that innervate  
extrafusal muscle fibres that  
generate force.

GAMMA MOTOR NEURON  
Motor neurons that innervate  
intrafusal muscle fibres  
associated with muscle spindles.

these domains. Activity in M1 has been linked to motor behaviour or to the motor periphery, but it has been difficult to reconcile a dual role for representing high-level aspects of motor performance such as hand trajectory and low-level details of motor execution.

Optimal feedback control, with its selective and highly adaptable feedback laws, provides an interesting model for describing how coordinated motor behaviour can be created by the motor system. The argument put forward here is that optimal feedback control can also

be of value for interpreting the neural basis of movement and in particular, neural processing in M1. Optimal feedback control is consistent with several aspects of neural processing in M1. Individual neurons contribute to the control of a portion of the motor periphery and receive rich, adaptable sensory feedback. The link between M1 and motor behaviour emerges through its contribution to the entire neural circuit. Therefore, the role of M1 is not 'muscles' versus 'movement', but muscles and movement.

1. Scott, S. H. Role of motor cortex in coordinating multi-joint movements: is it time for a new paradigm? *Can. J. Physiol. Pharmacol.* **78**, 923–933 (2000).
2. Hill, A. V. The heat of shortening and the dynamic constants of muscle. *Proc. R. Soc. Lond. B* **126**, 136–195 (1938).
3. Gordon, A. M., Huxley, A. F. & Julian, F. J. The variation in isometric tension with sarcomere length in vertebrate muscle fibres. *J. Physiol. (Lond.)* **184**, 170–192 (1966).
4. Burke, R. E., Levine, D. N., Tsairis, P. & Zajac, F. E. Physiological types and histochemical profiles in motor units of the cat gastrocnemius. *J. Physiol. (Lond.)* **234**, 723–748 (1973).
5. Scott, S. H., Brown, I. E. & Loeb, G. E. Mechanics of feline soleus: I. effect of fascicle length and velocity on force output. *J. Muscle Res. Cell Motil.* **17**, 207–219 (1996).
6. Cheng, E. J., Brown, I. E. & Loeb, G. E. Virtual muscle: a computational approach to understanding the effects of muscle properties on motor control. *J. Neurosci. Methods* **101**, 117–130 (2000).
7. Zajac, F. E. Muscle and tendon: properties, models, scaling, and application to biomechanics and motor control. *Crit. Rev. Biomed. Eng.* **17**, 359–411 (1989).
8. Otten, E. in *Exercise and Sport Sciences Reviews* (ed. Pandolf, K. B.) 89–137 (Williams & Wilkins, Baltimore, 1989).
9. Cheng, E. J. & Scott, S. H. Morphometry of *Macaca mulatta* forelimb. I. Shoulder and elbow muscles and segment inertial parameters. *J. Morphol.* **245**, 206–224 (2000).
10. Singh, K., Melis, E. H., Richmond, F. J. & Scott, S. H. Morphometry of *Macaca mulatta* forelimb. II. Fiber-type composition in shoulder and elbow muscles. *J. Morphol.* **251**, 323–332 (2002).
11. Graham, K. M. & Scott, S. H. Morphometry of *Macaca mulatta* forelimb. III. Moment arm of shoulder and elbow muscles. *J. Morphol.* **255**, 301–314 (2003).
12. Hollerbach, J. M. & Flash, T. Dynamic interactions between limb segments during planar arm movement. *Biol. Cybern.* **44**, 67–77 (1982).
13. Zajac, F. E. & Gordon, M. E. in *Exercise and Sport Sciences Reviews* (ed. Pandolf, K. B.) 187–230 (Williams & Wilkins, Baltimore, 1989).
14. Mussa-Ivaldi, F. A., Hogan, N. & Bizzi, E. Neural, mechanical, and geometric factors subserving arm posture in humans. *J. Neurosci.* **5**, 2732–2743 (1985).
15. Graham, K. M. *et al.* Kinematics and kinetics of multi-joint reaching in non-human primates. *J. Neurophysiol.* **89**, 2667–2677 (2003).
16. Schieber, M. H., Gardinier, J. & Liu, J. Tension distribution to the five digits of the hand by neuromuscular compartments in the macaque flexor digitorum profundus. *J. Neurosci.* **21**, 2150–2158 (2001).
17. Valero-Cuevas, F. J., Johanson, M. E. & Towles, J. D. Towards a realistic biomechanical model of the thumb: the choice of kinematic description may be more critical than the solution method or the variability/uncertainty of musculoskeletal parameters. *J. Biomech.* **36**, 1019–1030 (2003).
18. Munhall, K. G. in *Dynamic Models of Motor Planning* (ed. Culicover, P.) 192–198 (Nature Publishing Group, London, 2002).
19. Morasso, P. Spatial control of arm movements. *Exp. Brain Res.* **42**, 223–227 (1981).
20. Flash, T. & Hogan, N. The coordination of arm movements: an experimentally confirmed mathematical model. *J. Neurosci.* **5**, 1688–1703 (1985).
21. Knylwo, A. M. & Rymer, W. Z. Role of intrinsic muscle properties in producing smooth movements. *IEEE Trans. Biomed. Eng.* **44**, 165–176 (1997).
22. Won, J. & Hogan, N. Stability properties of human reaching movements. *Exp. Brain Res.* **107**, 125–136 (1995).
23. Lackner, J. R. & DiZio, P. Rapid adaptation to coriolis force perturbations of arm trajectory. *J. Neurophysiol.* **72**, 299–313 (1994).
24. Shadmehr, R. & Mussa-Ivaldi, F. A. Rapid adaptation to coriolis force perturbations of arm trajectory. *J. Neurosci.* **14**, 3208–3224 (1994).

**References 23 and 24 are classic studies that illustrate how subjects modify motor commands to compensate for mechanical loads applied to the limb during reaching.**

25. Flanagan, J. R. & Rao, A. K. Trajectory adaptation to a nonlinear visuomotor transformation: evidence of motion planning in visually perceived space. *J. Neurophysiol.* **74**, 2174–2178 (1995).
26. Sainburg, R. L., Ghez, C. & Kalakanis, D. Intersegmental dynamics are controlled by sequential anticipatory, error correction, and postural mechanisms. *J. Neurophysiol.* **81**, 1045–1056 (1999).
27. Flanagan, J. R., Vetter, P., Johansson, R. S. & Wolpert, D. M. Prediction precedes control in motor learning. *Curr. Biol.* **13**, 146–150 (2003).
28. Singh, K. & Scott, S. H. A motor learning strategy reflects neural circuitry for limb control. *Nature Neurosci.* **6**, 399–403 (2003).
29. Scott, S. H. & Loeb, G. E. The computation of position sense from spindles in mono- and multiarticular muscles. *J. Neurosci.* **14**, 7529–7540 (1994).
30. Harris, C. M. & Wolpert, D. M. Signal-dependent noise determines motor planning. *Nature* **394**, 780–784 (1998).

**This study illustrates how optimal strategies for minimizing signal-dependent noise lead to bell-shaped velocity profiles and relatively straight hand trajectories.**

31. Valbo, A. B. Human muscle spindle discharge during isometric voluntary contractions. Amplitude relations between spindle frequency and torque. *Acta Physiol. Scand.* **90**, 319–336 (1974).
32. Winter, D. A. Kinematic and kinetic patterns in human gait: variability and compensating effects. *Hum. Mov. Sci.* **3**, 51–76 (1984).
33. Lacquaniti, F. & Maioli, C. Coordinate transformations in the control of cat posture. *J. Neurophysiol.* **72**, 1496–1515 (1994).
34. Scholz, J. P. & Schoner, G. The uncontrolled manifold concept: identifying control variables for a functional task. *Exp. Brain Res.* **126**, 289–306 (1999).
35. Scholz, J. P., Schoner, G. & Latash, M. L. Identifying the control structure of multi-joint coordination during pistol shooting. *Exp. Brain Res.* **135**, 382–404 (2000).
36. Sabes, P. N., Jordan, M. I. & Wolpert, D. M. The role of inertial sensitivity in motor planning. *J. Neurosci.* **18**, 5948–5957 (1998).
37. Kording, K. P. & Wolpert, D. M. Bayesian integration in sensorimotor learning. *Nature* **427**, 244–247 (2004).
38. Todorov, E. & Jordan, M. I. Optimal feedback control as a theory of motor coordination. *Nature Neurosci.* **5**, 1226–1235 (2002).

**This study illustrates how optimal feedback control can predict many features of volitional motor control, including muscle synergies, motor coordination and variable but accurate movements.**

39. Todorov, E. Cosine tuning minimizes motor errors. *Neural Comput.* **14**, 1233–1260 (2002).
40. van Beers, R. J., Haggard, P. & Wolpert, D. M. The role of execution noise in movement variability. *J. Neurophysiol.* **91**, 1050–1063 (2004).
41. Christel, M. I. & Billard, A. Comparison between macaques' and humans' kinematics of prehension: the role of morphological differences and control mechanisms. *Behav. Brain Res.* **131**, 169–184 (2002).
42. Porter, R. & Lemon, R. N. *Cortical Function and Voluntary Movement* (Clarendon, Oxford, 1993).
43. Hepp-Reymond, M. C. Functional organization of motor cortex and its participation in voluntary movements. *Comp. Primate Biol.* **4**, 501–624 (1988).
44. Wise, S. P., Di Pellegrino, G. & Boussaoud, D. The premotor cortex and nonstandard sensorimotor mapping. *Can. J. Physiol. Pharmacol.* **74**, 469–482 (1996).
45. Gribble, P. L. & Scott, S. H. Overlap of internal models in motor cortex for mechanical loads during reaching. *Nature* **417**, 938–941 (2002).
46. Iriki, A., Tanaka, M., Iwamura, Y. Coding of modified body schema during tool use by macaque postcentral neurones. *Neuroreport* **7**, 2325–2330 (1996).

**The first in a series of studies to show how neural activity related to the hand is modified when monkeys are trained to use a rake to retrieve food rewards.**

47. Wise, S. P., Boussaoud, D., Johnson, P. B. & Caminiti, R. Premotor and parietal cortex: corticocortical connectivity and combinatorial computations. *Annu. Rev. Neurosci.* **20**, 25–42 (1997).
48. Battaglia-Mayer, A., Caminiti, R., Lacquaniti, F. & Zago, M. Multiple levels of representation of reaching in the parieto-frontal network. *Cereb. Cortex* **13**, 1009–1022 (2003).
49. Rizzolatti, G. & Luppino, G. The cortical motor system. *Neuron* **31**, 889–901 (2001).
50. Kalaska, J. F., Scott, S. H., Cisek, P. & Sergio, L. E. Cortical control of reaching movements. *Curr. Opin. Neurobiol.* **7**, 849–859 (1997).
51. Tanji, J. Sequential organization of multiple movements: involvement of cortical motor areas. *Annu. Rev. Neurosci.* **24**, 631–651 (2001).
52. Hoffman, D. S. & Strick, P. L. Effects of a primary motor cortex lesion on step-tracking movements of the wrist. *J. Neurophysiol.* **73**, 891–895 (1995).
53. Dum, R. P. & Strick, P. L. Spinal cord terminations of the medial wall motor areas in macaque monkeys. *J. Neurosci.* **16**, 6513–6525 (1996).
54. Fetz, E. E. & Cheney, P. D. Postspike facilitation of forelimb muscle activity by primate corticomotoneuronal cells. *J. Neurophysiol.* **44**, 751–772 (1980).
55. Shinoda, Y., Yokota, J. & Futami, T. Divergent projection of individual corticospinal axons to motoneurons of multiple muscles in the monkey. *Neurosci. Lett.* **23**, 7–12 (1981).
56. Lawrence, D. G., Porter, R. & Redman, S. J. Corticomotoneuronal synapses in the monkey: light microscopic localization upon motoneurons of intrinsic muscles of the hand. *J. Comp. Neurol.* **232**, 499–510 (1985).
57. McKiernan B. J., Marcario J. K., Karrer J. H. & Cheney P. D. Correlations between corticomotoneuronal (CM) cell postspike effects and cell-target muscle covariation. *J. Neurophysiol.* **83**, 99–115 (2000).
58. Heffner, R. & Masterton, B. Variation in form of the pyramidal tract and its relationship to digital dexterity. *Brain Behav. Evol.* **12**, 161–200 (1975).
59. Nakajima, K., Maier, M. A., Kirkwood, P. A. & Lemon, R. N. Striking differences in transmission of corticospinal excitation to upper limb motoneurons in two primate species. *J. Neurophysiol.* **84**, 698–709 (2000).
60. Gordon, J. G., Ghilardi, M. F. & Ghez, C. Accuracy of planar reaching movements. I. Independence of direction and extent variability. *Exp. Brain Res.* **99**, 97–111 (1994).
61. Moran, D. W. & Schwartz, A. B. Motor cortical representation of speed and direction during reaching. *J. Neurophysiol.* **82**, 2676–2692 (1999).
62. Soechting, J. F. & Flanders, M. Moving in three-dimensional space: frames of reference, vectors, and coordinate systems. *Annu. Rev. Neurosci.* **15**, 167–191 (1992).
63. Kalaska, J. F. & Crammond, D. J. Cerebral cortical mechanisms of reaching movements. *Science* **255**, 1517–1523 (1992).
64. Georgopoulos, A. P., Kalaska J. F., Caminiti, R. & Massey, J. T. On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex. *J. Neurosci.* **2**, 1527–1537 (1982).

65. Georgopoulos, A. P., Caminiti, R., Kalaska, J. F. & Massey, J. T. Spatial coding of movement: a hypothesis concerning the coding of movement directions by motor cortical populations. *Exp. Brain Res. (Suppl.)* **7**, 327–336 (1983).
66. Fu, Q. G., Flament, D., Coltz, J. D. & Ebner, T. J. Temporal encoding of movement kinematics in the discharge of primate primary motor and premotor neurons. *J. Neurophysiol.* **73**, 836–854 (1995).
67. Schwartz, A. B. Motor cortical activity during drawing movements: population representation during sinusoid tracing. *J. Neurophysiol.* **70**, 28–36 (1993).
68. Kalaska, J. F., Caminiti, R. & Georgopoulos, A. P. Cortical mechanisms related to the direction of two-dimensional arm movements: relations in parietal area 5 and comparison with motor cortex. *Exp. Brain Res.* **51**, 247–260 (1983).
69. Cohen, D. A., Prud'homme, M. J. & Kalaska, J. F. Tactile activity in primate primary somatosensory cortex during active arm movements: correlation with receptive field properties. *J. Neurophysiol.* **71**, 161–172 (1994).
70. Caminiti, R., Johnson, P. B., Galli, C., Ferraina, S. & Burnod, Y. Making arm movements within different parts of space: the premotor and motor cortical representation of a coordinate system for reaching to visual targets. *J. Neurosci.* **11**, 1182–1197 (1991).
71. Fortier, P. A., Smith, A. M. & Kalaska, J. F. Comparison of cerebellar and motor cortex activity during reaching: directional tuning and response variability. *J. Neurophysiol.* **69**, 1136–1149 (1993).
72. Bosco, G. & Poppele, R. E. Modulation of dorsal spinocerebellar responses to limb movement. II. Effect of sensory input. *J. Neurophysiol.* **90**, 3372–3383 (2003).
73. Jones, K. E., Wessberg, J. & Valbo, A. B. Directional tuning of human forearm muscle afferents during voluntary wrist movements. *J. Physiol. (Lond.)* **536**, 635–647 (2001).
74. Ribot-Ciscar, E., Bergenheim, M., Albert, F. & Roll, J. P. Proprioceptive population coding of limb position in humans. *Exp. Brain Res.* **149**, 512–519 (2003).
75. Kalaska, J. F., Cohen, D. A., Hyde, M. L. & Prud'homme, M. A comparison of movement direction-related versus load direction-related activity in primate motor cortex, using a two-dimensional reaching task. *J. Neurosci.* **9**, 2080–2102 (1989).
76. Scott, S. H. & Kalaska, J. F. Reaching movements with similar hand paths but different arm orientations: I. Activity of individual cells in motor cortex. *J. Neurophysiol.* **77**, 826–852 (1997).
77. Georgopoulos, A. P. Current issues in directional motor control. *Trends Neurosci.* **18**, 506–510 (1995).
78. Georgopoulos, A. P. On the translation of directional motor cortical commands to activation of muscles via spinal interneuronal systems. *Cogn. Brain Res.* **3**, 151–155 (1996).
79. Fukson, O. I., Berkinblit, M. B. & Feldman, A. G. The spinal frog takes into account the scheme of its body during the wiping reflex. *Science* **209**, 1261–1263 (1980).
80. Kargo, W. J. & Giszter, S. F. Afferent roles in hind limb wipe-reflex trajectories: free-limb kinematics and motor patterns. *J. Neurophysiol.* **83**, 1480–1501 (2000).
81. D'Avella, A., Saltiel, P. & Bizzi, E. Combinations of muscle synergies in the construction of a natural motor behavior. *Nature Neurosci.* **6**, 300–308 (2003).
82. Georgopoulos, A. P. & Ashe, J. One motor cortex, two different views. *Nature Neurosci.* **3**, 963–965 (2000).
83. Moran, D. W. & Schwartz, A. B. One motor cortex, two different views. *Nature Neurosci.* **3**, 963–965 (2000).
84. Todorov, E. Reply to 'One motor cortex, two different views'. *Nature Neurosci.* **3**, 963–964 (2000).
85. Scott, S. H. Reply to 'One motor cortex, two different views'. *Nature Neuroscience* **3**, 964–965 (2000).
86. Mussa-Ivaldi, F. A. Do neurons in the motor cortex encode movement direction? An alternative hypothesis. *Neurosci. Lett.* **91**, 106–111 (1988).
87. Todorov, E. Direct cortical control of muscle activation in voluntary arm movements: a model. *Nature Neurosci.* **3**, 391–398 (2000).
88. Sanger, T. D. Neural population codes. *Curr. Opin. Neurobiol.* **13**, 238–249 (2003).
89. Scott, S. H., Gribble, P. L., Graham, K. M. & Cabel, D. W. Dissociation between hand motion and population vectors from neural activity in motor cortex. *Nature* **413**, 161–165 (2001).
90. Scott, S. H. The role of primary motor cortex in goal-directed movements: insights from neurophysiological studies on non-human primates. *Curr. Opin. Neurobiol.* **13**, 671–677 (2003).
91. Miall, R. C., Weir, D. J., Wolpert, D. M. & Stein, J. Is the cerebellum a smith predictor? *J. Motor Behav.* **25**, 203–216 (1993).
92. Scott, S. H. & Norman, K. E. Computational approaches to motor control and their potential role for interpreting motor dysfunction. *Curr. Opin. Neurol.* **16**, 693–698 (2003).
93. Holdefer, R. N. & Miller, L. E. Primary motor cortical neurons encode functional muscle synergies. *Exp. Brain Res.* **146**, 233–243 (2002).
94. Bennett, K. M. & Lemon, R. N. Corticomotoneuronal contribution to the fractionation of muscle activity during precision grip in the monkey. *J. Neurophysiol.* **75**, 1826–1842 (1996).
95. Sergio, L. E. & Kalaska, J. F. Systematic changes in motor cortex cell activity with arm posture during directional isometric force generation. *J. Neurophysiol.* **89**, 212–228 (2003).
96. Kakei, S., Hoffman, D. S. & Strick, P. L. Muscle and movement representations in the primary motor cortex. *Science* **285**, 2136–2139 (1999).
97. Passingham, R. E. Premotor cortex: sensory cues and movement. *Behav. Brain Res.* **18**, 175–185 (1985).
98. Passingham, R. E., Chen, Y. C. & Thaler, D. in *Neural Programming* (ed. Ito, M.) 13–24 (Karger, Basel, 1989).
99. Kurata, K. & Hoffman, D. S. Differential effects of muscimol microinjection into dorsal and ventral aspects of the premotor cortex of monkeys. *J. Neurophysiol.* **71**, 1151–1164 (1994).
100. Kurata, K. & Hoshi, E. Reacquisition deficits in prism adaptation after muscimol microinjection into the ventral premotor cortex of monkeys. *J. Neurophysiol.* **81**, 1927–1938 (1999).
101. Schmidt, E. M., Porter, R. & McIntosh, J. S. The effects of cooling supplementary motor area and midline cerebral cortex on neuronal responses in area 4 of monkeys. *Electroencephalogr. Clin. Neurophysiol.* **85**, 61–71 (1992).
102. Sparks, D. L. The brainstem control of saccadic eye movements. *Nature Rev. Neurosci.* **3**, 952–964 (2002).
103. Scudder, C. A., Kaneko, C. S. & Fuchs, A. F. The brainstem burst generator for saccadic eye movements: a modern synthesis. *Exp. Brain Res.* **142**, 439–462 (2002).
104. Robinson, D. A. in *Basic Mechanisms of Ocular Motility and Their Clinical Implications* (eds Lennerstrand, G. & Bach-y-Rita, P.) 337–374 (Pergamon, Oxford, 1975).
105. Gallana, H. L. & Guittion, D. Central organization and modeling of eye-head coordination during orienting gaze shifts. *Ann. NY Acad. Sci.* **656**, 452–471 (1992).
106. Houk, J. C. in *Cerebral Motor Control in Man: Long Loop Mechanisms*. (ed. Desmedt, J. E.) 193–215 (Karger, Basel, 1978).
107. Loeb, G. E. Hard lessons in motor control from the mammalian spinal cord. *Trends Neurosci.* **10**, 108–113 (1987).
108. Feldman, A. G. & Levin, M. The origin and use of positional frames of reference in motor control. *Behav. Brain Sci.* **18**, 724–807 (1995).
109. Hinder, M. R. & Milner, T. E. The case for an internal dynamics model versus equilibrium point control in human movement. *J. Physiol. (Lond.)* **549**, 953–963 (2003).
110. Bullock, D., Grossberg, S. & Guenther, F. H. A self-organizing neural model of motor equivalent reaching and tool use by a multi-joint arm. *J. Cogn. Neurosci.* **5**, 408–435 (1993).
111. Cisek, P., Grossberg, S. & Bullock, D. A cortico-spinal model of reaching and proprioception under multiple task constraints. *J. Cogn. Neurosci.* **10**, 425–444 (1998).
112. Pandy, M. G. & Zajac, F. E. Optimal muscular coordination strategies for jumping. *J. Biomech.* **24**, 1–10 (1991).
113. Uno, Y., Kawato, M. & Suzuki, R. Formation and control of optimal trajectory in human multi-joint arm movement. Minimum torque-change model. *Biol. Cybern.* **61**, 89–101 (1989).
114. Hoff, B. & Arbib, M. A. Models of trajectory formation and temporal interaction of reach and grasp. *J. Motor Behav.* **25**, 175–192 (1993).
115. Hogan, N. An organizing principle for a class of voluntary movements. *J. Neurosci.* **4**, 2745–2754 (1984).
116. Dingwell, J. B., Mah, C. D. & Mussa-Ivaldi, F. A. Experimentally confirmed mathematical model for human control of a non-rigid object. *J. Neurophysiol.* **91**, 1158–1170 (2004).
- This study illustrates how the motor system calculates state variables not only related to body motion, but also related to motion of grasped non-rigid objects.**
117. He, J., Levine, W. S. & Loeb, G. E. Feedback gains for correcting small perturbations to standing posture. *IEEE Trans. Automatic Control* **36**, 322–332 (1991).
- One of the first examples of the use of optimal control methods to identify feedback gains, in this case, for spinal reflexes in the cat hindlimb.**
118. Kuo, A. D. An optimal control model for analyzing human postural balance. *IEEE Trans. Biomed. Eng.* **42**, 87–101 (1995).
119. Meyer, D. E., Abrams, R. A., Kornblum, S., Wright, C. E. & Smith, J. E. Optimality in human motor performance: ideal control of rapid aimed movements. *Psychol. Rev.* **95**, 340–370 (1988).
120. Jeka, J. J. & Lackner, J. R. Fingertip contact influences human postural control. *Exp. Brain Res.* **100**, 495–502 (1994).
121. Stengel, R. F. *Optimal Control and Estimation* (Dover, New York, 1994).
122. Wolpert, D. M., Ghahramani, Z. & Jordan, M. I. An internal model for sensorimotor integration. *Science* **269**, 1880–1882 (1995).
123. Gordon, J. & Ghez, C. Trajectory control in targeted force impulses. III. Compensatory adjustments for initial errors. *Exp. Brain Res.* **67**, 253–269 (1987).
124. Pearson, K. G. Proprioceptive regulation of locomotion. *Curr. Opin. Neurobiol.* **5**, 786–791 (1995).
125. Scott, S. H. Population vectors and motor cortex: neural coding or epiphenomenon? *Nature Neurosci.* **3**, 307–308 (2000).
126. Sanes, J. N. & Schieber, M. H. Orderly somatotopy in primary motor cortex: does it exist? *Neuroimage* **13**, 968–974 (2001).
127. Park, M. C., Belhaj-Saif, A., Gordon, M. & Cheney, P. D. Consistent features in the forelimb representation of primary motor cortex in rhesus macaques. *J. Neurosci.* **21**, 2784–2792 (2001).
128. Cabel, D. W., Cisek, P. & Scott, S. H. Neural activity in primary motor cortex related to mechanical loads applied to the shoulder and elbow during a postural task. *J. Neurophysiol.* **86**, 2102–2108 (2001).
129. Wong, Y. C., Kwan, H. C., MacKay, W. A. & Murphy, J. T. Spatial organization of precentral cortex in awake primates. I. Somatosensory inputs. *J. Neurophysiol.* **41**, 1107–1119 (1978).
130. Scott, S. H. Comparison of onset time and magnitude of activity for proximal arm muscles and motor cortical cells prior to reaching movements. *J. Neurophysiol.* **77**, 1016–1022 (1997).
131. Murphy, J. T., Wong, Y. C. & Kwan, H. C. Sequential activation of neurons in primate motor cortex during unrestrained forelimb movement. *J. Neurophysiol.* **53**, 435–445 (1985).
132. Lemon, R. N. Functional properties of monkey motor cortex neurones receiving afferent input from the hand and fingers. *J. Physiol. (Lond.)* **311**, 497–519 (1981).
133. Strick, P. L. & Preston, J. B. Sorting of somatosensory afferent information in primate motor cortex. *Brain Res.* **156**, 364–368 (1978).
134. Picard, N. & Smith, A. M. Primary motor cortical activity related to the weight and texture of grasped objects in the monkey. *J. Neurophysiol.* **68**, 1867–1881 (1992).
135. Armstrong, D. M. & Drew, T. Topographical localization in the motor cortex of the cat for somatic afferent responses and evoked movements. *J. Physiol. (Lond.)* **350**, 33–54 (1984).
136. Wolpaw, J. R. Correlations between task-related activity and responses to perturbation in primate sensorimotor cortex. *J. Neurophysiol.* **44**, 1122–1138 (1980).
137. Fromm, C. in *Motor Control Mechanisms in Health and Disease* (ed. Desmedt, J. E.) 329–345 (Raven, New York, 1983).
138. Lemon, R. N. & Porter, R. Afferent input to movement-related precentral neurones in conscious monkeys. *Proc. R. Soc. Lond. B* **194**, 313–339 (1976).
139. Evars, E. V. & Fromm, C. in *Cerebral Motor Control in Man: Long Loop Mechanisms* (ed. Desmedt, J. E.) 178–192 (Karger, Basel, 1978).
140. Matthews, P. B. The human stretch reflex and the motor cortex. *Trends Neurosci.* **14**, 87–91 (1991).
141. Soechting, J. F. & Lacquaniti, F. Quantitative evaluation of the electromyographic responses to multidirectional load perturbations of the human arm. *J. Neurophysiol.* **59**, 1296–1313 (1988).
142. Burdet, E., Osu, R., Franklin, D. W., Milner, T. E. & Kawato, M. The central nervous system stabilizes unstable dynamics by learning optimal impedance. *Nature* **414**, 446–449 (2001).
143. Wang, T., Dordevic, G. S. & Shadmehr, R. Learning the dynamics of reaching movements results in the modification of arm impedance and long-latency perturbation responses. *Biol. Cybern.* **85**, 437–448 (2001).
144. Meyer-Lohmann, J., Conrad, B., Matsunami, K. & Brooks, V. B. Effects of dentate cooling on precentral unit activity following torque pulse injections into elbow movements. *Brain Res.* **94**, 237–251 (1975).
145. Conrad, B. in *Cerebral Motor Control in Man: Long Loop Mechanisms* (ed. Desmedt, J. E.) 123–140 (Karger, Basel, 1978).
146. Vilis, T., Hore, J., Meyer-Lohmann, J. & Brooks, V. B. Dual nature of the precentral responses to limb perturbations revealed by cerebellar cooling. *Brain Res.* **117**, 336–340 (1976).
147. Strick, P. L. The influence of motor preparation on the response of cerebellar neurons to limb displacements. *J. Neurosci.* **3**, 2007–2020 (1983).
148. Strick, P. L. in *Cerebral Motor Control in Man: Long Loop Mechanisms*. (ed. Desmedt, J. E.) 85–93 (Karger, Basel, 1978).

149. Pellissier, D., Prablanc, C., Goodale, M. A. & Jeannerod, M. Visual control of reaching movements without vision of the limb: II. Evidence of fast, unconscious processes correcting the trajectory of the hand to the final position of a double-step stimulus. *Exp. Brain Res.* **62**, 303–311 (1986).
150. Prablanc, C. & Martin, O. Automatic control during hand reaching at undetected two-dimensional target displacements. *J. Neurophysiol.* **67**, 455–469 (1992).
151. Desmurget, M. & Grafton, S. Forward modeling allows feedback control for fast reaching movements. *Trends Cogn. Sci.* **4**, 423–431 (2000).
152. Shen, L. & Alexander, G. E. Neural correlates of a spatial sensory-to-motor transformation in primary motor cortex. *J. Neurophysiol.* **77**, 1171–1194 (1997).
153. Desmurget, M. *et al.* Role of the posterior parietal cortex in updating reaching movements to a visual target. *Nature Neurosci.* **2**, 563–567 (1999).
154. Grea, H. *et al.* A lesion of the posterior parietal cortex disrupts on-line adjustments during aiming movements. *Neuropsychologia* **40**, 2471–2480 (2002).
155. Bossom, J. Movement without proprioception. *Brain Res.* **71**, 285–296 (1974).
156. Taub, E., Goldberg, I. A. & Taub, P. Deafferentation in monkeys: pointing at a target without visual feedback. *Exp. Neurol.* **46**, 178–186 (1975).
157. Sainburg, R. L., Ghilardi, M. F., Poizner, H. & Ghez, C. Control of limb dynamics in normal subjects and patients without proprioception. *J. Neurophysiol.* **73**, 820–835 (1995).
158. Desmedt, J. E. *Cerebral Motor Control in Man: Long Loop Mechanisms* (Karger, Basel, 1978).
159. Tanji, J. & Evarts, E. V. Anticipatory activity of motor cortex neurons in relation to direction of an intended movement. *J. Neurophysiol.* **5**, 1062–1068 (1976).
160. Prut, Y. & Fetz, E. E. Primate spinal interneurons show pre-movement instructed delay activity. *Nature* **401**, 590–594 (1999).
161. Goodale, M. A. & Milner, A. D. Separate visual pathways for perception and action. *Trends Neurosci.* **15**, 20–25 (1992).
162. Cohen, Y. E. & Andersen, R. A. A common reference frame for movement plans in the posterior parietal cortex. *Nature Rev. Neurosci.* **3**, 553–562 (2002).
163. Cisek, P. & Kalaska, J. F. In *The Handbook of Brain Theory and Neural Networks* (ed. Arbib, M. A.) 945–948 (The MIT Press, Cambridge, 2003).
164. Thach, W. T., Goodkin, H. P. & Keating, J. G. The cerebellum and the adaptive coordination of movement. *Annu. Rev. Neurosci.* **15**, 403–442 (1992).
165. Ito, M. *The Cerebellum and Neural Control* (Raven, New York, 1984).
166. Kawato, M. in *The Handbook of Brain Theory and Neural Networks* (ed. Arbib, M. A.) 190–195 (The MIT Press, Cambridge, 2003).
167. Houk, J. C., Keifer, J. & Barto, A. G. Distributed motor commands in the limb premotor network. *Trends Neurosci.* **16**, 27–33 (1993).
168. Bastian, A. J. Cerebellar limb ataxia: abnormal control of self-generated and external forces. *Ann. NY Acad. Sci.* **978**, 16–27 (2002).
169. Wolpert, D. M. & Kawato, M. Multiple paired forward and inverse models for motor control. *Neural Netw.* **11**, 1317–1329 (1998).
170. Dum, R. P. & Strick, P. L. An unfolded map of the cerebellar dentate nucleus and its projections to the cerebral cortex. *J. Neurophysiol.* **89**, 634–639 (2003).
- The use of retrograde transneuronal labelling with herpes virus from injections in different areas of the cerebral cortex shows that the dentate nucleus contains anatomically separate regions for motor and non-motor domains.**
171. Kelly, R. M. & Strick, P. L. Cerebellar loops with motor cortex and prefrontal cortex of a nonhuman primate. *J. Neurosci.* **23**, 8432–8444 (2003).
172. Evarts, E. V. & Tanji, J. Reflex and intended responses in motor cortex pyramidal tract neurons of monkey. *J. Neurophysiol.* **39**, 1069–1080 (1976).
173. Seki, K., Perimutter, S. I. & Fetz, E. E. Sensory input to primate spinal cord is presynaptically inhibited during voluntary movement. *Nature Neurosci.* **6**, 1309–1316 (2003).
174. Loeb, G. E., Brown, I. E. & Cheng, E. J. A hierarchical foundation for models of sensorimotor control. *Exp. Brain Res.* **126**, 1–18 (1999).
175. Todorov, E. & Li, W. Optimal control methods suitable for biomechanical systems. *Proc. 25th Ann. Int. Conf. IEEE Eng. Biol. Med. Soc.* **2**, 1758–1761 (2003).
176. Marr, D. *Vision* (Freeman, San Francisco, 1982).
177. Barto, A. in *The Handbook of Brain Theory and Neural Networks* (ed. Arbib, M. A.) 968–972 (The MIT Press, Cambridge, 2003).
178. Kawato, M. Internal models for motor control and trajectory planning. *Curr. Opin. Neurobiol.* **9**, 718–727 (1999).
179. Doya, K. Complementary roles of basal ganglia and cerebellum in learning and motor control. *Curr. Opin. Neurobiol.* **10**, 732–739 (2000).
180. Sanes, J. N. Neocortical mechanisms in motor learning. *Curr. Opin. Neurobiol.* **13**, 225–231 (2003).
181. Li, C. S., Padoa-Schioppa, C. & Bizzi, E. Neuronal correlates of motor performance and motor learning in the primary motor cortex of monkeys adapting to an external force field. *Neuron* **30**, 593–607 (2001).
182. Paz, R., Boraid, T., Natan, C., Bergman, H. & Vaadia, E. Preparatory activity in motor cortex reflects learning of local visuomotor skills. *Nature Neurosci.* **6**, 882–890 (2003).
183. Wise, S. P., Moody, S. L., Blomstrom, K. J. & Mitz, A. R. Changes in motor cortical activity during visuomotor adaptation. *Exp. Brain Res.* **121**, 285–299 (1998).
184. Kuypers, H. G. J. M. in *Handbook of Physiology* Sec. 1 Vol. II (ed. Brooks, V. B.) 597–666 (American Physiological Society, Chicago, 1981).
185. Murray, E. A. & Coulter, J. D. Organization of corticospinal neurons in the monkey. *J. Comp. Neurol.* **195**, 339–365 (1981).
186. Lackner, J. R. & DiZio, P. A. Aspects of body self-calibration. *Trends Cogn. Sci.* **4**, 279–288 (2000).
187. Scott, S. H. Optimal strategies for movement: success with variability. *Nature Neurosci.* **5**, 1110–1111 (2002)

#### Acknowledgements

This research was supported by research grants from the Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council of Canada. I am also supported by a CIHR Investigator Award. I would also like to acknowledge expert technical support from K. Moore and J. Swaine, as well as constructive criticisms on this manuscript from P. K. Rose, D. P. Munoz, I. Kurtzer, T. Herter and other members of the CIHR Group in Sensorimotor Research.

#### Competing interests statement

The author declares **competing financial interests**: see web version for details.

#### Online links

#### FURTHER INFORMATION

**Encyclopedia of Life Sciences:** [http://www.els.net/motor\\_neurons\\_and\\_spinal\\_control\\_of\\_movement|motor\\_output\\_from\\_the\\_brain\\_and\\_spinal\\_cord|motor\\_system\\_organization|proprioceptive\\_sensory\\_feedback](http://www.els.net/motor_neurons_and_spinal_control_of_movement|motor_output_from_the_brain_and_spinal_cord|motor_system_organization|proprioceptive_sensory_feedback)  
**Scott's laboratory homepage:** <http://anatomy.queensu.ca/faculty/scott.cfm>  
**Access to this interactive links box is free online.**